

## REMARKS

### 35 U.S.C. § 101

Claims 1, 2 and 9 were rejected under 35 U.S.C. 101 for encompassing non-statutory subject matter, i.e., a transgenic human being. The claims have been amended to encompass a transgenic mouse whose genome comprises knockouts in Gpx 1 and Gpx 2.

In view of the foregoing amendments and remarks, it is respectfully submitted that the claims as amended satisfy the provisions of 35 U.S.C. 101 and withdrawal of the rejection of claims for encompassing non-statutory subject matter is requested.

### *35 U.S.C. 112, 1<sup>st</sup> paragraph rejections*

Claims 1-25, 40-49 and 60-63 were rejected under 35 U.S.C. 112, first paragraph, for lack of enablement. The Examiner is of the opinion that the claims are enabled for a transgenic mouse whose genome comprises homozygous disruption of both *Gpx1* and *Gpx2*, wherein the mouse exhibits the disclosed phenotypes. However, the Examiner goes on to assert that the specification is not enabling for other transgenic animals that are encompassed by claims 1-2, 9 and 16. The claims have been amended or canceled where appropriate to recite a transgenic mouse whose genome comprises homozygous disruption of *Gpx1* and/or *Gpx2*.

Claims 1-25, 40-49, and 60-63 were rejected for lack of enablement because the Examiner is of the opinion that the specification provides working examples of double knockout mice with a phenotype selected from the following: ileitis, colitis, decreased weight gain, hypothermia, perianal ulceration, diarrhea, wasting syndrome, inflammatory bowel disease, dysplasia of the small bowel and tumors of the small bowel. The Examiner has asserted, however, that some of the claims are directed to broader phenotypes than those disclosed, such as the development of

cancer, one or more signs or symptoms associated with cancer, ileal cancer, myeloleukemia and cancer of the lower gastrointestinal tract. The Examiner is of the opinion that claims to this broader class of phenotypes are not enabled.

In order to maintain a rejection for lack of enablement, the Examiner must provide specific technical reasoning as to why the claimed invention is not enabled. As apparent technical reasoning for the assertion of non-enablement, the Examiner has cited Moreadith et al., as disclosing that one of skill could not predict the phenotype of a knockout mouse, and Moens, et al., Development, 1993, Vol. 119, pages 485-499, for disclosing that two different positional mutations in N-myc produce two different phenotypes in mouse ES cells (one “leaky” and one “null”). The Examiner is thus of the opinion that it would be “difficult” to predict any phenotype resulting from a double knockout as in the present invention.

In response to the above assertion, Applicants respectfully submit that the phenotype of tumors is explicitly disclosed in the Examples and the tumors are indicative of cancer and other signs and symptoms associated with cancer, as well known in the art. It is respectfully submitted that the cited references do not provide the specific technical reasoning necessary to establish that mice who develop tumors do not develop cancer or display the signs and symptoms associated with cancer (such as, e.g., tumors).

The Examiner is also of the opinion that the specification discloses that mice which are heterozygous for a disruption one of the GPX genes and homozygous for a disruption of the other GPX gene do not “exhibit a phenotype” (Office Action at page 7). Based on this assertion, the Examiner is of the opinion that claims 40 and 60-63, as written, are not enabled, since they appear as wildtype and do not include a phenotype that differs from the wildtype mouse. With regard to claim 40, the claim is to a double homozygous mouse with a phenotype different from

wildtype, i.e., decreased levels of GPX-I and GPX-GI protein production. Applicants thus submit that this ground of rejection is inapplicable to claim 40. With regard to claims 60-63, as stated both within the claims and also at pages 31-32, these mice provide a valuable model for the study of the functional redundancy of GPX1 and GPX-GI in various tissues.

In view of the foregoing amendments and remarks, it is respectfully submitted that the claims as amended satisfy the provisions of 35 U.S.C. 112, first paragraph and withdrawal of the claims for lack of enablement is requested.

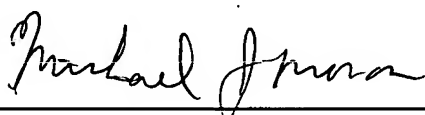
*35 U.S.C. §112, 2<sup>nd</sup> paragraph rejections*

Claims 1-8 and 19 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite. Claim 1 recites a disruption of the “*Gpx1* gene and *Gpx2* genes.” The Examiner has required correction and claim 1 has been amended to recite a singular *Gpx2* gene. Claim 19 was rejected for being unclear as written, since it recites a model of claim 18, when claim 18 in fact is directed to a method, not a model. Claim 19 has been amended to recite the method of claim 18.

In view of the foregoing amendments and remarks, it is respectfully submitted that the claims as amended satisfy the provisions of 35 U.S.C. 112, second paragraph and withdrawal of the claims for being indefinite is requested.

### CONCLUSION

In view of the above amendments and remarks, it is believed that the claims satisfy the requirements of the patent statutes and reconsideration of the instant application and early notice of allowance are requested. The Examiner is invited to telephone the undersigned if it is deemed to expedite allowance of the application.

RESPECTFULLY SUBMITTED,			
	Michael J. Moran, Ph.D., Registration No. 42,013		
SIGNATURE		DATE	5/29/03

Address	Rothwell, Figg, Ernst & Manbeck Suite 800, 1425 K Street, N.W.				
City	Washington	State	D.C.	Zip Code	20005
Country	U.S.A.	Telephone	202-783-6040	Fax	202-783-6031